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EXAMINER	
STAPLES, MARK	

ART UNIT	PAPER NUMBER
1637	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/516,744	TRINQUET ET AL.	
	Examiner	Art Unit	
	Mark Staples	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04/11/2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-41* is/are pending in the application.

4a) Of the above claim(s) *7-13 and 31-41* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 14-30* is/are rejected.

7)☒ Claim(s) *18* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *06 December 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/06/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of claim 1 in part, claims 2-6, and claims 14-30 of Group I in the reply filed on 4/11/2007 is acknowledged. The traversal is on the ground(s) that that there is little additional burden to examine the first 9 groups of claims as claim 1 encompasses each of these groups in part. This is not found persuasive because the groups lack the same or corresponding technical feature and thus do not form a single inventive concept and owing to the different subject matter in the groups it would be a serious search burden to examine all groups together.

The requirement is still deemed proper and is therefore made FINAL.

Claims 7-13 and 31-41 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected group, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 4/11/2007.

Information Disclosure Statement

2. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a

separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Specification

3. The use of the trademark BODIPY® has been noted in this application. It and any other trademarks should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Objections

4. Claim 18 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The oligonucleotides of claim 17 by definition are the element of claim 18, that is, a series of ribonucleotide or dexoribonucleotide units attached to one another via phosphodiester bonds.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-6 and claims 14-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 recites the pronoun "it" in line 3. What this pronoun refers to is unclear as several antecedent things are recited. Thus what comprises the fluorescent entity of claim 1 is unclear. Consequently dependent claims 2-6 and 14-30 are also unclear.

6. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949).

In the present instance, claim 4 recites the broad recitation "a high molecular extinction coefficient, greater than 20,000", and the claim also recites "preferably greater than 50,000" which is the narrower statement of the range/limitation.

In the present instance, claim 17 recites the broad recitation "from 5 to 60" nucleotide units, and the claim also recites "in particular 5 to 20, preferably from 5 to 15 nucleotide units" which is the narrower statement of the range/limitation.

7. Claim 5 contains the trademark/trade name BODIPY®. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe fluorophores and, accordingly, the identification/description is indefinite.

8. Claim 27 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 27 recites the term "the sequence A_{15}". It is unknown what this is and the specification does not provide clarification. It is noted the specification does refer to CY5™-A15-cAMP but there is no apparent connection with this entity and "the sequence A_{15}".

9. Claim 28 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between

the elements. See MPEP § 2172.01. The omitted elements are: the elements of the molar ratio. It is unknown and hence indefinite as to what is ratio of what else.

10. Claim 28 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. See MPEP § 2172.01. The omitted structural cooperative relationships are: what parameters are used to calculate the final molar ratio. There are at least four parameters recited in antecedent claim 27, a conjugate, a fluorophore, an oligonucleotide, and a carrier molecule. It is unclear which, if any of these, is used to determine the final molar ratio.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 1-6, 14, 15, and 17-24 are rejected under 35 U.S.C. 102(b) as being anticipated by Glazer et al. (US Patent No. 5,853,992 issued 1998).

Regarding claim 1, Glazer et al. teach an oligonucleotide comprising a fluorophore (entire patent, especially claims 1 and 12) which can have at least one

functional group, for example the amide bond of a spacer arm (see the structure at column 8, lines 14-22 and see claim 27).

Regarding claims 2, 17, and 18, Glazer et al. teach an oligonucleotide of 5 to 30 nucleotides in length which is within the range of 2 to 60 nucleotides in length (see claim 14).

Regarding claim 3 and 14, Glazer et al. teach where the fluorophore is attached via a spacer arm (see claim 27).

Regarding claim 4, Glazer et al. teach where the fluorophore has aromatic rings and has a molar extinction coefficient of greater than 60,000 M^{-1} cm^{-1} (see column 3 lines 9-38).

Regarding claim 5, Glazer et al. teach where the fluorophore is a cyanin dye (see column 3 lines 9-38).

Regarding claims 6 and 22, Glazer et al. teach where the fluorophore has a carboxy group, carboxylic acid (see claims 21 and 22).

Regarding claim 14, Glazer et al. teach where the fluorophore is covalently attached to the oligonucleotide through a spacer arm (see the structure at column 8, lines 14-22 and see claim 27).

Regarding claim 15 and 24, Glazer et al. teach a liner spacer arm having a divalent organic radical which can be of the length of C_1-C_{20} and containing one hetero atom, N (see the structure at column 8, lines 14-22 and see claim 27).

Regarding claim 19, Glazer et al. teach phosphoroamide bonds in a phosphoroamidite method (see column 12 lines 61-67).

Regarding claims 20-23, Glazer et al. teach the synthesis of the N-hydroxysuccinimide ester of cyanine dyes (see the section beginning at column 11 line 10) which is then joined to a free amine space on an oligonucleotide analog/nucleoside analog (see the section Design and Synthesis of ET Primers beginning at column 12 line 33). The oligonucleotide has at least 5 internucleotide phosphodiester bonds at the end used for attachment to the fluorophore (see the oligonucleotide sequence at column 12 line 65).

12. Claims 1-3, 14, 17, 18, and 26-30 are rejected under 35 U.S.C. 102(b) as being anticipated by Tyagi et al. (US Patent No. 5,925,517 issued 1999).

Regarding claim 1, Tyagi et al. teach an oligonucleotide comprising a fluorophore (entire patent, especially claim 1) and can have functional groups, amide bonds, introduced through linage to a spacer arm which is an octapeptide (see column 17 line 10).

Regarding claims 2, 17, and 18, Tyagi et al. teach an oligonucleotide of 3 to 15 nucleotides in length which is within the range of 2 to 60 nucleotides in length (see claim 8).

Regarding claim 3 and 14, Tyagi et al. teach where the fluorophore is attached via a spacer arm (see claims 22 and 110).

Regarding claim 14, Tyagi et al. teach where the fluorophore is covalently attached to the fluorophore through a spacer arm (entire patent, especially claims 1-27).

Regarding claims 26-30, Tyagi et al. teach a fluorophore-nucleotide conjugate covalently attached to an antibody, the antibody here interpreted as the carrier molecule as (see Figure 1 and its detailed description found at column 9 line 2 through to column 11 line 21). The molar ratio of claim 28 is interpreted to be the molar ratio of the fluorophore-nucleotide conjugate to the antibody. By definition, this molar ratio must be at least 1, as at least one fluorophore-nucleotide conjugate molecule must be covalently linked to at least one antibody molecule. Tyagi et al. thus inherently teach a molar ratio of at least 1.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

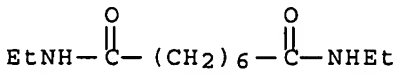
13. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

14. Claims 16 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Glazer et al. as applied to claims 1, 14, 15, and 24 above, and further in view of Surrey et al. (US Patent 3,143,566 issued 1964).

Glazer et al. teach as noted above.

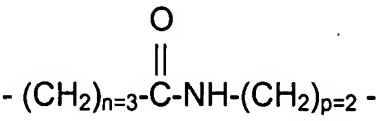
Glazer et al. do not specifically teach a spacer arm of the structures given in claims 16 and 25.

Surrey et al. specifically teach structure 3 of claims 16 and 25 by teaching alkyl diamides and specifically where n=2 in structure 3, Surrey et al. teach N,N'-diethyl octanediamide, CAS Registry No. 91565-14-9, as shown below:



Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the spacer arm of Glazer et al. by using N,N'-diethyl octanediamide which is a 20 atom linking arm as suggested by Surrey et al. with a reasonable expectation of success. The motivation to do so is provided by Glazer et al. who teach the 20 atom length specifically for use with oligonucleotides: "Linkage of the fluorophores to the backbone is achieved by conventional covalent binding. . . .In the case of nucleic acid backbones [oligonucleotides], linkage is preferably achieved by use of a convenient linking arm usually consisting of from about 2 to about 20 . . . atoms" (see column 7 line 65 through to column 8 line 9). Glazer et al.

further teach: "A preferred linking group structure is an amide-containing chain . . . (see column 8 lines 10-111). Glazer et al. then teach the exact half of N,N'-diethyl octanediamide by teaching the structure:



which is N ethyl butanamide (see column 8 lines 14-22). It is noted that combining two of these to achieve the 20 atom length gives the structure of Surrey et al. Glazer et al. also teach where there are two amide groups in a linear spacer arm (see Figure 1). From the teachings of Glazer et al. one would be motivated to use various spacer arms of 20 atoms, preferably those including amide groups, and thus preferably including the specific and known one taught by Surrey et al. Thus the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

Conclusion

15. No claim is free of the prior art.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Staples whose telephone number is (571) 272-9053. The examiner can normally be reached on Monday through Thursday, 9:00 a.m. to 7:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Mark Staples MS
Examiner
Art Unit 1637
May 11, 2007

TERESA E. STRZELECKA, PH.D.
PRIMARY EXAMINER

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5/11/07